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Doyon, L. / Tremblay, S. / Bourgon, L. / Wardrop, E. / Cordingley, M.G., *Antiviral Research*, Oct 2005
...Construction of recombinant HIV-1 The proviral DNA used to produce WT HIV-1 was plasmid 2.12, an HIV-1 encoding pNL4.3 plasmid (NIH **AIDS** Research and Reference Reagent Program) (Adachi et al., 1986), modified to contain a unique Bst1107I site at codon 125 of the...
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Jianmin Duan / Josie De Marte / William Paris / Diana Roopchand / Tamara L Fleet / Jo-Anne Clarke / Siu-Hong Yeong / (...) / Michael G Cordingley, *Antiviral Res*, Dec 2004
...grafting to NIH-nu-bg-xid mice under halothane anesthesia. Cutaneous xenografts were dressed with antibiotics and protective band-**aids** for 3 weeks. In the paralleled experiment using the same viral stock containing both HPV6 and 11, and matched grafts, no visible...
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Duan, J. / Marte, J.D. / Paris, W. / Roopchand, D. / Fleet, T.L. / Clarke, J.-A. / Yeong, S.-H. / (...) / Cordingley, M.G., *Antiviral Research*, Dec 2004
...grafting to NIH-nu-bg-xid mice under halothane anesthesia. Cutaneous xenografts were dressed with antibiotics and protective band-**aids** for 3 weeks. In the paralleled experiment using the same viral stock containing both HPV6 and 11, and matched grafts, no visible...
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Garneau, M. / Bolger, G.T. / Bousquet, C. / Kibler, P. / Tremblay, F. / Cordingley, M.G., *Antiviral Research*, Aug 2003
...up to 40% of patients with acquired immunodeficiency syndrome (**AIDS**) were at risk to develop progressive retinal destruction leading...mice (Duan et al., 1994), while retrovirally induced murine **AIDS** (MAIDS) led to a higher incidence of necrotizing retinopathy...
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CORDINGLEY, Michael, Graham / BOEHRINGER INGELHEIM INTERNATIONAL GMBH, *PATENT COOPERATION TREATY APPLICATION*, Jul 2004
...HIV-1) which results in acquired immunodeficiency syndrome (**AIDS**) and related diseases. For this indication, the compound of the...and low dose ritonavir an attractive drug 10 combination for **AIDS** therapy. Those skilled in the art would know how to formulate...
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Bolger, G. / Lapeyre, N. / Rheaume, M. / Kibler, P. / Bousquet, C. / Garneau, M. / Cordingley, M., *Antiviral Research*, Dec 1999
...transplant, organ transplant followed by immunosuppressive therapy or **AIDS** (Betts, 1997). Mild CMV infection and rarely, severe CMV infection...hepatitis and acalculous cholecystitis have also been noted in **AIDS** patients (Drew, 1988 Pollard, 1988 Betts, 1997), while rare...
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☐ **7.** Experiences from the Structure Determination of Human Cytomegalovirus Protease
Tong, L. / Qian, C. / Davidson, W. / Massariol, M.-J. / Bonneau, P.R. / Cordingley, M.G. / Lagacé, L., *Acta Crystallographica Section D: Biological Crystallography*, Nov 1997
...infections are clinically asymptomatic (Fields & Knipe, 1990). However, in immunosuppressed and immunocompromised individuals (**AIDS** patients and organ-transplant recipients), HCMV infections can cause severe health problems and even death (Fields & Knipe, 1990...
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☐ **8.** A new serine-protease fold revealed by the crystal structure of human cytomegalovirus protease.
L Tong / C Qian / M J Massariol / P R Bonneau / M G Cordingley / L Lagacé, *Nature*, Sep 1996
...population in the United States and can cause morbidity and mortality in immunosuppressed individuals (organ-transplant recipients and **AIDS** patients) and congenitally infected newborns. hCMV protease is essential for the production of mature infectious virions, as...
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...mutabon in tlte UL97 gene produt-t in a HCMV isolate from an **AIDS** pabenL F. Baldanti', A. Sarasini', L simoncini', M. Zavanoni...mone frequently detected in the clinical senings. A patient witb **AIDS** and HCMV retinitis was submined to virological follow-up and...
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☐ **10.** Lethal Hepatitis During Acute MCMV Infection: Analysis and Treatment With Ganciclovir and HPMPC.
Bolger, G. / Lapeyre, N. / Garneau, M. / Rheaume, M. / Kibler, P. / Bousquet, C. / Cordingley, M.G., *Antiviral Research*, Apr 1997
...mutabon in tlte UL97 gene produt-t in a HCMV isolate from an **AIDS** pabenL F. Baldanti', A. Sarasini', L simoncini', M. Zavanoni...mone frequently detected in the clinical senings. A patient witb **AIDS** and HCMV retinitis was submined to virological follow-up and...
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L1   ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:445778  HCAPLUS
DOCUMENT NUMBER:          144:468213
TITLE:                    Process for preparation of diazepine N-oxide
```

derivatives as non-nucleoside HIV-1 reverse transcriptase inhibitors

INVENTOR(S): Meyer, Oliver; Heddesheimer, Ingo; Zerban, Georg

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gmbh & Co. KG, Germany

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006048425	A1	20060511	WO 2005-EP55706	20051102
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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US 2006100200	A1	20060511	US 2005-264281	20051101
PRIORITY APPLN. INFO.:			EP 2004-26241 A	20041105

OTHER SOURCE(S): MARPAT 144:468213

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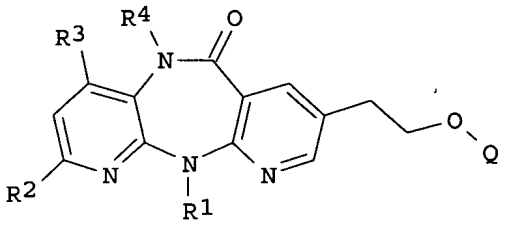

I

ABSTRACT:
The invention provides a process for preparing N-oxides of diazepine derivs. I [wherein R1 = Me, Et, cyclopropyl, Pr, iso-Pr, or cyclobutyl; R2 = H, F, Cl, alkyl, cycloalkyl, or CF3; R3 = H or Me, R4 = H, Me, or Et; Q = 1-oxido-4-quinolinyl or 1-oxido-5-quinolinyl] or pharmaceutically acceptable salts thereof, comprising oxidation of the corresponding diazepine derivs. under phase-transfer conditions. For example, I (R1 = Et; R2 and R3 = H; R4 = Me; Q = 4-quinolinyl) was treated with OXONE in CH2Cl2/water in the presence of tetrabutylammonium hydrogensulfate and acetone to give I (R1 = Et; R2 and R3 = H; R4 = Me; Q = 1-oxido-4-quinolinyl) with 99.3% purity. The title compds. are effective inhibitors of HIV reverse transcriptase (no data).

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L1 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1078236 HCAPLUS
DOCUMENT NUMBER: 143:353310
ENTRY DATE: Entered STN: 07 Oct 2005
TITLE: Crystalline forms of 5, 11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy}ethyl}-6H-dipyrido[3,2-b:2',3'-e] [1,4]diazepin-6-one and methods for preparation
INVENTOR(S): Busacca, Carl A.; Cerretà, Michael; Varsolona, Richard; Smoliga, John; Lorenz, Jon; Vitous, Jana
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany
SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-551
SECONDARY: C07D487-14
US PATENT CLASSIF.: 514220000; 540495000
CLASSIFICATION: 63-5 (Pharmaceuticals)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005222134	A1	20051006	US 2005-83401	20050318
WO 2005097796	A2	20051020	WO 2005-US9655	20050323
WO 2005097796	A3	20060105		

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PRIORITY APPLN. INFO.: US 2004-559354P P 20040402
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2005222134	ICM	A61K031-551
	ICS	C07D487-14
	INCL	514220000; 540495000
	IPCI	A61K0031-551 [ICM,7]; C07D0487-14 [ICS,7]; C07D0487-00 [ICS,7,C*]
	IPCR	A61K0031-551 [I,A]; A61K0031-551 [I,C*]; C07D0487-00 [I,C*]; C07D0487-14 [I,A]
	NCL	514/220.000
	ECLA	C07D471/14+245B+221B+221B
WO 2005097796	IPCI	C07D0471-14 [ICM,7]; C07D0471-00 [ICM,7,C*]; A61K0031-551 [ICS,7]; A61P0031-18 [ICS,7]; A61P0031-00 [ICS,7,C*]
	IPCR	A61K0031-551 [I,A]; A61K0031-551 [I,C*]; C07D0471-00 [I,C*]; C07D0471-14 [I,A]

ABSTRACT:
The present invention comprises the discovery of a dihydrate crystalline form of 5,11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy}ethyl}

-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one, which is thermodynamically or kinetically favored at temps. and humidity's that are most likely to be encountered upon storage of drug substance or drug product and thus pharmaceutically preferred to the trihydrate that is provided by the prior art. The invention also comprises methods for making this dihydrate crystalline form. The invention further discovers that under proper conditions several anhydrous polymorphs of 5,11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy} ethyl}-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one may be formed. One of these, which is designated as anhydrous Form III (AF III), has demonstrated phase stability at some tested ambient conditions, which indicates that it is pharmaceutically acceptable, and biol. testing has shown that it leads to higher plasma levels than are attainable using other crystalline forms of the drug. Thus, the invention further includes anhydrous Form III of 5,11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy}ethyl} -6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one and methods for its manufacture

SUPPL. TERM: cryst form anhyd diazepin dihydrate prepn
INDEX TERM: Anti-AIDS agents
Powder x-ray diffractometry
(crystalline forms of 5, 11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy}ethyl}-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one and methods for preparation)
INDEX TERM: Human immunodeficiency virus 1
(reverse transcriptase inhibitor, treatment of; crystalline forms of 5, 11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy}ethyl}-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one and methods for preparation)
INDEX TERM: 380378-81-4 865887-44-1
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystalline forms of 5, 11-dihydro-11-ethyl-5-methyl-8-{2-{(1-oxido-4-quinolinyl)oxy}ethyl}-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one and methods for preparation)

L1 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:531365 HCAPLUS
DOCUMENT NUMBER: 141:65063
ENTRY DATE: Entered STN: 02 Jul 2004
TITLE: Use of a combination containing a non-nucleoside reverse transcriptase inhibitor (NNRTI) with an inhibitor of cytochrome p450 for the treatment of HIV-1 infection
INVENTOR(S): Cordingley, Michael Graham
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-55
SECONDARY: A61K031-00; A61K031-427; A61P031-18
CLASSIFICATION: 1-5 (Pharmacology)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054586	A1	20040701	WO 2003-EP14224	20031215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

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CA 2510143	AA	20040701	CA 2003-2510143		20031215
AU 2003296647	A1	20040709	AU 2003-296647		20031215
US 2004152625	A1	20040805	US 2003-736301		20031215
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BR 2003017095	A	20051025	BR 2003-17095		20031215
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PRIORITY APPLN. INFO.:			US 2002-433690P	P	20021216
			WO 2003-EP14224	W	20031215

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004054586	ICM	A61K031-55
	ICS	A61K031-00; A61K031-427; A61P031-18
	IPCI	A61K0031-55 [ICM,7]; A61K0031-00 [ICS,7]; A61K0031-427 [ICS,7]; A61P0031-18 [ICS,7]; A61P0031-00 [ICS,7,C*]
	IPCR	A61K0031-352 [I,C*]; A61K0031-353 [I,A]; A61K0031-427 [I,A]; A61K0031-427 [I,C*]; A61K0031-55 [I,A]; A61K0031-55 [I,C*]; A61K0031-551 [I,A]; A61K0031-551 [I,C*]; A61K0031-554 [I,A]; A61K0031-554 [I,C*]; A61K0031-7042 [I,C*]; A61K0031-7048 [I,A]; A61K0038-12 [I,C*]; A61K0038-13 [I,A]
	ECLA	A61K031/353+M; A61K031/427+M; A61K031/55+M; A61K031/551+M; A61K031/554+M; A61K031/7048+M; A61K035/78+M; A61K038/13+M
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US 2004152625	IPCI	A61K0038-13 [ICM,7]; A61K0038-12 [ICM,7,C*]; A61K0031-7048 [ICS,7]; A61K0031-7042 [ICS,7,C*]; A61K0031-551 [ICS,7]; A61K0031-554 [ICS,7]; A61K0031-353 [ICS,7]; A61K0031-352 [ICS,7,C*]
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JP 2006511538	IPCI	A61K0031-551 [I,A]; A61K0045-00 [I,A]; A61K0031-427 [I,A]; A61P0031-18 [I,A]; A61P0031-00 [I,C*]; A61P0043-00 [I,A]
	FTERM	4C084/AA19; 4C084/MA17; 4C084/MA35; 4C084/MA37; 4C084/MA52; 4C084/MA55; 4C084/MA59; 4C084/MA63; 4C084/MA66; 4C084/NA05; 4C084/NA14; 4C084/ZB331; 4C084/ZB332; 4C084/ZC202; 4C084/ZC551; 4C084/ZC552; 4C086/AA01; 4C086/AA02; 4C086/BC82; 4C086/CB11; 4C086/MA02; 4C086/MA04; 4C086/NA05; 4C086/NA14; 4C086/ZB33; 4C086/ZC20; 4C086/ZC55
NO 2005003455	IPCI	A61K0031-55 [ICM,7]; A61K0031-00 [ICS,7]; A61K0031-427 [ICS,7]; A61P0031-18 [ICS,7]; A61P0031-00 [ICS,7,C*]
	ECLA	A61K031/353+M; A61K031/427+M; A61K031/55+M; A61K031/551+M; A61K031/554+M; A61K031/7048+M; A61K035/78+M; A61K038/13+M

ABSTRACT:
An improved method for using a NNRTI in the treatment of HIV-1 infection comprises administering to a human in need of treatment for HIV-1 infection a therapeutically effective amount of the NNRTI, or a pharmaceutically acceptable salt thereof, and an amount of an inhibitor of cytochrome P 450 that is sufficient to elevate, enhance, or extend plasma concns. of said NNRTI.

SUPPL. TERM: nonnucleoside reverse transcriptase inhibitor cytochrome P450 inhibitor combination HIV1

INDEX TERM: AIDS (disease)
Anti-AIDS agents
Antiviral agents

Drug delivery systems
Drug metabolism
Grapefruit juice
Human
Human immunodeficiency virus
Human immunodeficiency virus 1
Pharmacokinetics
(non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

INDEX TERM: Drug interactions
(pharmacokinetic; non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

INDEX TERM: Infection
(viral; non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

INDEX TERM: 9035-51-2, Cytochrome P 450, biological studies
329322-82-9, Cytochrome P 450 3A
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

INDEX TERM: 380378-81-4
ROLE: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

INDEX TERM: 114-07-8, Erythromycin 1406-18-4, Vitamin E 7380-40-7, Bergamottin 42399-41-7, Diltiazem 65277-42-1, Ketoconazole 79217-60-0, Cyclosporin 81103-11-9, Clarithromycin 83366-66-9, Nefazodone 84625-61-6, Itraconazole 116644-53-2, Mibefradil 145414-76-2 150378-17-9, Indinavir 155213-67-5, Ritonavir 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 198904-31-3, Atazanavir 380378-81-4D, mixts. with grapefruit juice 710282-28-3 710282-29-4 710282-30-7 710282-31-8 710282-32-9 710282-33-0 710282-34-1 710282-35-2 710282-36-3 710282-37-4 710282-38-5 710282-39-6 710282-40-9 710282-41-0 710282-42-1 710282-43-2
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-nucleoside reverse transcriptase inhibitor combination with cytochrome P 450 inhibitor for treatment of HIV-1 infection)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Barry, D; WO 9844913 A 1998 HCAPLUS
(2) Boehringer Ingelheim Ca Ltd; WO 0196338 A 2001 HCAPLUS
(3) Kaltenbach, R; US 6391919 B1 2002 HCAPLUS
(4) Malaty, L; DRUG SAFETY 1999, V20(2), P147 HCAPLUS

L1 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:923799 HCAPLUS
DOCUMENT NUMBER: 136:37632
ENTRY DATE: Entered STN: 21 Dec 2001
TITLE: Preparation of non-nucleoside reverse transcriptase

inhibitors
INVENTOR(S): Simoneau, Bruno
PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D471-14
SECONDARY: A61K031-55; C07D471-14; C07D243-00; C07D221-00; C07D221-00
CLASSIFICATION: 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096338	A1	20011220	WO 2001-CA890	20010614
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US 2002028807	A1	20020307	US 2001-879447	20010612
US 6420359	B2	20020716		
CA 2411766	AA	20011220	CA 2001-2411766	20010614
CA 2411766	C	20060523		
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NZ 523549	A	20040827	NZ 2001-523549	20010614
AT 322492	E	20060415	AT 2001-949124	20010614
EP 1655300	A1	20060510	EP 2006-100695	20010614
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BG 107348	A	20040630	BG 2002-107348	20021203
NO 2002005844	A	20021205	NO 2002-5844	20021205
HK 1057558	A1	20050408	HK 2004-100468	20040121

PRIORITY APPLN. INFO.:

US 2000-212329P	P	20000616
US 2000-256638P	P	20001218
EP 2001-949124	A3	20010614
WO 2001-CA890	W	20010614

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001096338	ICM	C07D471-14
	ICS	A61K031-55; C07D471-14; C07D243-00; C07D221-00; C07D221-00
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	IPCR	C07D0471-00 [I,C*]; C07D0471-14 [I,A]
	ECLA	C07D471/14+243B+221B+221B; C07D471/14+243+221+221
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	IPCR	C07D0471-00 [I,C*]; C07D0471-14 [I,A]
	NCL	514/220.000
	ECLA	C07D471/14+243B+221B+221B
CA 2411766	IPCI	A61K0031-55 [I,A]; C07D0221-00 [I,A]; C07D0243-00 [I,A]; C07D0471-14 [I,A]; C07D0471-00 [I,C*]
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	IPCR	C07D0471-00 [I,C*]; C07D0471-14 [I,A]
	ECLA	C07D471/14+243B+221B+221B; C07D471/14+243+221+221
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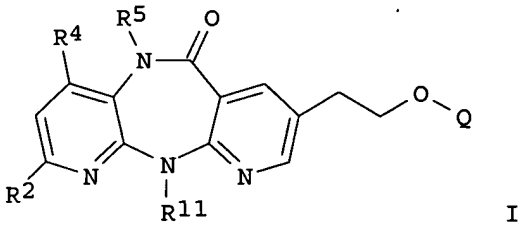

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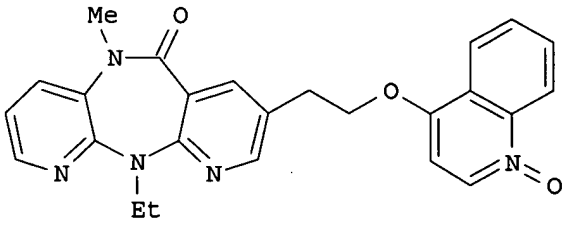

II

ABSTRACT:
Compds. of formula I [R2 = H, F, Cl, (C1-4) alkyl, (C3-4) cycloalkyl, CF3; R4 = H, Me; R5 = H, Me, Et; R4 and R5 are not both Me, and if R4 is Me then R5 cannot be Et; R11 = Et, cyclopropyl, Pr, iso-Pr, isobutyl; Q = 4- or 5-quinolinyl or their 1-oxides] are prepared as inhibitors of HIV reverse transcriptase, wild-type and several mutant strains. Thus, II was prepared in several steps from 2-chloro-3-nitropyridine, ethylamine, 5-bromo-2-chloro-3-pyridinecarbonyl chloride and 4-hydroxyquinoline. II was shown to inhibit wild-type and mutant strains of reverse transcriptase in assays.

SUPPL. TERM: dipyridodiazepinone deriv prepn reverse transcriptase inhibitor; HIV replication inhibitor dipyridodiazepinone deriv prepn

INDEX TERM: Anti-AIDS agents
(preparation of dipyridodiazepinone derivs. as inhibitors of HIV replication)

INDEX TERM: 9068-38-6, Reverse transcriptase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of dipyridodiazepinone derivs. as reverse transcriptase inhibitors)

INDEX TERM: 380378-62-1P 380378-63-2P 380378-64-3P 380378-65-4P
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380378-75-6P 380378-76-7P 380378-77-8P 380378-78-9P
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380379-39-5P
ROLE: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dipyridodiazepinone derivs. as reverse transcriptase inhibitors)

INDEX TERM: 578-67-6, 5-Hydroxyquinoline 611-36-9, 4-Hydroxyquinoline 765-30-0, Cyclopropylamine 1513-65-1, 2,6-Difluoropyridine 2393-23-9, 4-Methoxybenzylamine 5470-18-8, 2-Chloro-3-nitropyridine 16013-85-7, 2,6-Dichloro-3-nitropyridine 17129-06-5, 4-Ethoxy-1,1,1-trifluoro-3-buten-2-one 24850-33-7, Allyltributyltin 26163-29-1

39745-40-9 49609-84-9, 2-Chloronicotinyl chloride
78686-86-9 129432-25-3 380379-38-4
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dipyridodiazepinone derivs. as reverse transcriptase inhibitors)

INDEX TERM: 26820-65-5P 32282-06-7P 33742-69-7P 58602-02-1P
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380378-93-8P 380378-94-9P 380378-95-0P 380378-96-1P
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380379-16-8P 380379-18-0P 380379-19-1P 380379-20-4P
380379-21-5P 380379-22-6P 380379-23-7P 380379-24-8P
380379-25-9P 380379-26-0P 380379-27-1P 380379-28-2P
380379-29-3P 380379-30-6P 380379-31-7P 380379-32-8P
380379-33-9P 380379-34-0P 380379-35-1P 380379-36-2P
380379-37-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dipyridodiazepinone derivs. as reverse transcriptase inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Cywin, C; J MED CHEM 1998, V41(16), P2972 HCAPLUS

=> S E5
L2 1 380378-81-4D/BI

=> DIS L2 1 TI

L2 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN
TI Use of a combination containing a non-nucleoside reverse transcriptase inhibitor (NNRTI) with an inhibitor of cytochrome p450 for the treatment of HIV-1 infection

=> S E6
L3 2 380378-81-4P/BI

=> DIS L3 1- TI
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):Y

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
TI Process for preparation of diazepine N-oxide derivatives as non-nucleoside HIV-1 reverse transcriptase inhibitors

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
TI Preparation of non-nucleoside reverse transcriptase inhibitors

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Basic Search Advanced Search Search Preferences

"reverse transcriptase inhibitors" AND ("combination tl Search

Journal sources Preferred Web sources Other Web sources Exact phrase

Searched for:: :All of the words:**"reverse transcriptase inhibitors"** AND (**"combination therapy"** AND **rito**

Found:: :**96 total** | **21 journal results** | **7 preferred web results** | **68 other web results**

Sort by:: :**relevance** | **date**

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1. Simple and rapid quantification of the non-nucleoside reverse transcriptase inhibitors nevirapine, delavirdine, and...
Rezk, N.L. / Tidwell, R.R. / Kashuba, A.D.M., *Journal of Chromatography B, Analytical Technologies in the Biomedical and Life Sciences*, Jul 2002
...quantification of the **non-nucleoside reverse transcriptase inhibitors** nevirapine...**non-nucleoside reverse transcriptase inhibitors** (nevirapine...**non-nucleoside reverse transcriptase inhibitors** proved to...activity of, the **cytochrome** P450 enzyme...consequences of **combination therapy** with NNRTIs...
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2. Metabolic complications associated with antiretroviral therapy
Jain, R.G. / Furfine, E.S. / Pedneault, L. / White, A.J. / Lenhard, J.M., *Antiviral Research*, Sep 2001
...NRTIs and **non-nucleoside reverse transcriptase**...nucleoside **reverse transcriptase inhibitors** (NRTIs), **non-nucleoside reverse transcriptase inhibitors** (NNRTIs...Nucleoside **reverse transcriptase inhibitors** inhibitors...Norvir(R)/**Ritonavir** (RTV) Viracept...
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3. Antiretroviral therapy of HIV-1 infection: established treatment strategies and new therapeutic options
Kaufmann, G.R. / Cooper, D.A., *Current Opinion in Microbiology*, Oct 2000
...shown that **non-nucleoside reverse transcriptase inhibitors**, such as...regimens. Triple **combination therapy** that includes...analogue **reverse transcriptase inhibitors** (nRTIs...saquinavir/**ritonavir** and saquinavir...investigations. 6 **Non-nucleoside** analogue **reverse transcriptase inhibitors** An alternative...lamivudine **combination**

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Stein, A.J. / Brothers, C.H. / Scott, T.R., *Clinical Therapeutics*, Mar 2001
...an inhibitor of the **cytochrome** P450 isoenzyme 3A4 (**CYP** 3A4), **ritonavir** in low doses (eg...Both amprenavir and **ritonavir** are substrates and...amprenavir 600 mg BID plus **ritonavir** 100 mg BID delivers...in the absence of **non-nucleoside reverse transcriptase inhibitors**-is appropriate when...Meta-analysis of triple **combination therapy** in antiretroviral...
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Menendez-Arias, L., *Trends in Pharmacological Sciences*, Aug 2002
...V82A, I84V, L90M h **Ritonavir** L10I/R/V, K20M/R...virus type 1 NNRTIs, **non-nucleoside reverse transcriptase inhibitors** PR, protease RT, reverse...administration of low doses of **ritonavir**, which significantly...elimination by the hepatic **cytochrome** P450 enzyme system...coadministration with **ritonavir**. **Combination therapy** and multidrug-resistant...
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Bonfanti, P. / Capetti, A. / Rizzardini, G., *Biomedicine & Pharmacotherapy*, Mar 1999
...PIs) or **non-nucleoside reverse transcriptase inhibitors** (NNRTIs...trial on **combination therapy** in advanced...Metabolism **cytochrome** P450 cyt...investigating **combination therapy** with two...such as **non- nucleoside reverse transcriptase inhibitors** (NNRTIs...
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De Clercq, E., *International Journal of Antimicrobial Agents*, Jun 1997
...saquinavir, **ritonavir**, indinavir...inhibitors: **Reverse transcriptase inhibitors** 1. Introduction...nucleoside **reverse transcriptase inhibitors** (NRTIs: AZT...d4T, 3TC), **non-nucleoside** reverse transcriptase...Clercq E. **Non-nucleoside reverse transcriptase inhibitors** (NNRTIs...of initial **combination therapy** with zidovudine...
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Bruno, R. / Sacchi, P. / Puoti, M. / Soriano, V. / Filice, G., *The American Journal of Gastroenterology*, Jul 2002
...i.e. , **ritonavir**) Immune reconstitution...nucleoside **reverse**

transcriptase inhibitors, acting as...effect on the **cytochrome** p450 isoenzyme...receiving **ritonavir** was no higher...patients. Among **non-nucleoside reverse transcriptase inhibitors**, nevirapine...

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BHIVA Guidelines Co-ordinating Committee / Gazzard, B. / Moyle, G. / Weber, J. / Johnson, M. / Bingham, J. / Brettle, R. / (...) / Griffin, G., *The Lancet*, Apr 1997
...Protease inhibitors **Non-nucleoside reverse transcriptase inhibitors** Zidovudine (ZDV, AZT...Zalcitabine (ddC) **Ritonavir** Delavirdine* Didanosine...nucleoside analogues plus a **non-nucleoside** reverse transcriptase...inhibitors Saquinavir+**ritonavir** Two nucleoside analogues...patients already on **combination therapy**. For these patients...that in late disease **ritonavir** will improve outcome...

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Spengler, U. / Lichterfeld, M. / Rockstroh, J.K., *Journal of Hepatology*, Feb 2002
...**inhibitors** (NRTI), **non-nucleoside reverse transcriptase inhibitors** (NNRTI) and...ng/ml) c **Cytochrome** P450 isoenzymes...Nucleoside **reverse transcriptase inhibitors** Zidovudine...**Non-nucleoside reverse transcriptase inhibitors** Delaviridine...CYP2C9, CYP2D6 **Ritonavir** Norvir (R...

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Warren Beach, J., *Clinical Therapeutics*, Jan 1998
...inhibitors (saquinavir, **ritonavir**, indinavir, and...drugs. Key words: **reverse transcriptase inhibitors**, protease inhibitors...Jersey). 14 the **CYP**-450 system by the...metabolism.,In addition, **ritonavir**, nelfinavir, delavirdine...saquinavir is limited to **combination therapy** because of the development...protease gene. 17,88 **Ritonavir** In contrast to saquinavir...In addition, the **CYP**-2D6 isoform contributes...

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Shafer, R.W. / Vuitton, D., *Biomedicine & Pharmacotherapy*, Mar 1999
...available HIV-I **non-nucleoside** RT inhibitors...Iâ€™450 **CYP** 3A enzymes...common muta- **CYP** IA enzymes...enzymes P236L **Non-nucleoside** RT inhibitors (NNRTI) The **non-nucleoside reverse transcriptase inhibitors** (NNRTI) inhibit...

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Rausch, D.M. / Stover, E.S., *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, Jan 2001
The human immunodeficiency virus invades the central nervous system early after infection where it later gives rise to cognitive, motor, and behavioral manifestations in children and adults.Ranging from mild impairments to frank...
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Aarnoutse, R.E. / Verweij-van Wissen, C.P.W.G.M. / Underberg, W.J.M. / Kleinnijenhuis, J. / Hekster, Y.A. / Burger, D.M., *Journal of Chromatography B: Biomedical Sciences and Applications*, Nov 2001
...nucleoside **reverse transcriptase inhibitors** (NRTIs) and **non-nucleoside reverse transcriptase inhibitors** (NNRTIs...nelfinavir, **ritonavir**, saquinavir...one of the **cytochrome** P450 iso...Especially **ritonavir** is a potent...applied in **combination therapy**. However...
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Swanstrom, R. / Erona, J., *Pharmacology and Therapeutics*, May 2000
...analogs. **Combination therapy** in which...nelfinavir NNRTI, **non-nucleoside** reverse transcriptase...transcriptase RTV, **ritonavir** SGC, soft...clinical use 150 **Ritonavir** 151 Indinavir...inhibitors in **combination therapy** 157 Protease...nucleoside analog **reverse transcriptase inhibitors** 157 The use...combined with **non-nucleoside reverse transcriptase inhibitors** 160 Salvage...
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Current Opinion in Biotechnology, Dec 1997
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Carr, A. / Cooper, D.A., *The Lancet*, Oct 2000
...nucleotide-analogue HIV **reverse-transcriptase inhibitors** Organ Features...lamivudine, NNRTI=**non-nucleoside** reverse transcriptase...Mouth ulcers **Non-nucleoside** analogues...formulation) **Ritonavir** Perioral paraesthesiae...paraesthesiae All **Cytochrome** P450 interaction...effective **combination therapy** Nat Med 5...effects of **reverse transcriptase inhibitors**:mitochondrial...
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Gopalakrishnan, R., *Antimicrobics and Infectious Diseases Newsletter*, Jul 1996
...superiority of **combination therapy** over monotherapy...approved for **combination therapy**. An attractive...agents are the **non-nucleoside** reverse transcriptase...in chronic **combination therapy** is yet to be...saquinavir, **ritonavir**, and indinavir...combination with **reverse transcriptase inhibitors**, it has resulted...
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Phenix, B.N. / Badley, A.D., *Biochimie*, Feb 2002
...molecule (vpr52-96) causes release of **cytochrome** c and apoptosis-inducing factor (AIF...followed by mitochondrial release of **cytochrome** c and cleavage of caspases 9 and 3...activation of these enzymes leads to **cytochrome** c release from mitochondria into the...
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Hernandez Conte, A.T., *Seminars in Anesthesia, Perioperative Medicine and Pain*, Dec 1998
...institution of **combination therapy** with reverse...Nucleoside **reverse transcriptase inhibitors** Zidovudine...Nonnucleoside **reverse transcriptase inhibitors** Nevirapine...Pharmaceuticals) **Ritonavir** (Norvir...bination with **reverse transcriptase inhibitors**. The most...the hepatic **cytochrome** P450 system...to AZT.22 **Ritonavir**.e3 **Ritonavir**...
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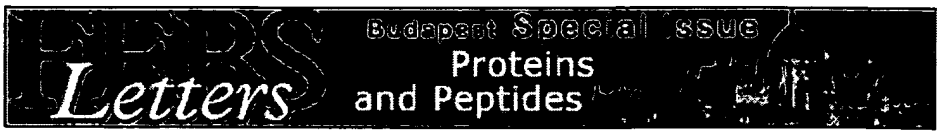

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Fung, H.B. / Stone, E.A. / Piacenti, F.J., *Clinical Therapeutics*, Oct 2002
...gained the attention of the HIV/**AIDS** community when Che-Chung Tsai...SIV), a primate model for **AIDS**. All macaques that received...meeting abstracts of major HIV/ **AIDS** conferences (1996-2002), using...substrates of the cytochrome P (**CYP**)-**450** enzymes.Z1 Although induction...amprenavir, indinavir, nelfinavir, **ritonavir**, and saquinavir) in MT-2 cells...
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Warren Beach, J., *Clinical Therapeutics*, Jan 1998
...for the treatment of **AIDS** (Figure 1). Zidovudine...Dermatologic Rash Bs **Ritonavir** CNS effects General weakness...metabolites are produced by the **CYP-450** 3A isozymes, but in vitro...New Jersey). 14 the **CYP-450** system by the 3A4 isoform...metabolism.,In addition, **ritonavir**, nelfinavir, delavirdine...
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Fung, H.B. / Kirschenbaum, H.L. / Hameed, R., *Clinical Therapeutics*, May 2000
...October 1996 (when most patients with **AIDS** were receivmg a protease in- hlbitor...significantly higher in patients with **AIDS** than in healthy individuals (27 ,LLM vs...concentratlons reported in patients with **AIDS** (27 WM). Based on thermodynamic and kmetic...inhibitors: indinavir, saquinavir, nelfinavir, **ritonavir**, and amprenavir. At trough

concentrations...

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Viard, J.-P. / Rouzioux, C., *Annales de l'Institut Pasteur/Actualites*, Jul 2000
...saquinavir, Invirase R et Fortovase **ritonavir**, NorvirW indinavir, Crixivan R nelfinavir...dans les urines) ? urinaire 45 hpatique (**CYP-450**) 0,4 hpatique (CYP3A4) 0,65-1,2hpatique...t bien tabli que de petites doses de **ritonavir** augmentent l aire sous la courbe du saquinavir...patienst receiving HIV protease rnhibitors, **AIDS** 12 (1998) F51-F58. 99 Le sX d re is StAir...

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Fung, H.B. / Stone, E.A. / Piacenti, F.J., *Clinical Therapeutics*, Oct 2002
...gained the attention of the HIV/**AIDS** community when Che-Chung Tsai...SIV), a primate model for **AIDS**. All macaques that received...meeting abstracts of major HIV/**AIDS** conferences (1996-2002), using...substrates of the cytochrome P (**CYP**)-**450** enzymes.Z1 Although induction...amprenavir, indinavir, nelfinavir, **ritonavir**, and saquinavir) in MT-2 cells...
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Warren Beach, J., *Clinical Therapeutics*, Jan 1998
...for the treatment of **AIDS** (Figure 1). Zidovudine...Dermatologic Rash Bs **Ritonavir**

CNS effects General weakness...metabolites are produced by the **CYP-450** 3A isozymes, but in vitro...New Jersey). 14 the **CYP-450** system by the 3A4 isoform...metabolism.,In addition, **ritonavir**, nelfinavir, delavirdine...

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Fung, H.B. / Kirschenbaum, H.L. / Hameed, R., *Clinical Therapeutics*, May 2000
...October 1996 (when most patients with **AIDS** were receivmg a protease in- hlbitor...significantly higher in patients with **AIDS** than in healthy individuals (27 ,LLM vs...concentratlons reported in patients with **AIDS** (27 WM). Based on thermodynamic and kmetic...inhibitors: indinavir, saquinavir, nelfinavir, **ritonavir**, and amprenavir. At trough concentrations...

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LEYLAND-JONES, Brian / MCGILL UNIVERSITY, *PATENT COOPERATION TREATY APPLICATION*, Nov 2002
The invention relates to the individualization of therapy on the basis of a phenotypic profile of an individual. More specifically, the present invention relates to the use of metabolic phenotyping for the individualization of treatment with...

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The invention relates to the individualization of therapy on the basis of a phenotypic profile of an individual. More specifically, the present invention relates to the use of metabolic phenotyping for the individualization of treatment with...

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☐ **16.** METABOLIC PHENOTYPING IN THERAPY WITH ANXIOLYTICS
LEYLAND-JONES, Brian / MCGILL UNIVERSITY, *PATENT COOPERATION TREATY APPLICATION*, Sep 2002

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☐ **18.** METABOLIC PHENOTYPING IN THERAPY WITH IMMUNOSUPPRESSANTS
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1. Pharmacologic Enhancement in Protease Inhibitor-based HAART: The Role of Ritonavir [132K]
Stephen L. Becker / Lorna Thornton, Sep 2004
...reason to justify their use. Adding **ritonavir**, however, is not without cost. Abnormalities...improvement rendered by the addition of **ritonavir**. Understanding the pharmacologic origins...malignancy, and a lowered incidence of any **AIDS**-defining diagnosis among patients with...enhancement of PI therapy (boosting) with **ritonavir**, itself an inhibitor of HIV protease...
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2. HIV & AIDS [PPT-2MB]
Feb 2006
...Hyperbilirubinemia Lopinavir/**Ritonavir** (Kaletra®, LPV/RTV) 3 capsules...Recommended for use in pregnancy **Ritonavir** (Norvir®, RTV) The "Booster...BREAK http://www.unfpa.org/**aids**_clock/main.htm 58 Resistance...Efavirenz 100-250 Saquinavir 2100 **Ritonavir** 800 Nelfinavir 1000 Lopinavir...Protease Inhibitors and NNRTIs **CYP 450** 3A4 Inhibitors and inducers...
[http://pharmacy.umkc.edu/New/pharm/PharmacotherapyIII/...]
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3. JOURNAL 7/02 [PDF-263K]
Aug 2002
...INTERNATIONAL ASSOCIATION OF PHYSICIANS IN **AIDS** CARE Headquarters Office Chicago, Illinois...INTERNATIONAL ASSOCIATION OF PHYSICIANS IN **AIDS** CARE Southern Africa Regional Office Johannesburg...International Association of Physicians in **AIDS** Care. All material published, including...
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4. Norvir, INN- Ritonavir [PDF-84K]
Oct 2005
...procedure. However a new formulation of **ritonavir**, Norvir 100 mg soft capsules has...further developed. Active substance **Ritonavir** is a chiral molecule. The enantiomeric...starting materials. Two polymorphs of **ritonavir** referred to as Forms I

and II are...
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☐ **5.** JOURNAL 7/02/YES [PDF-144K]
Dec 2002
...Combination therapy with indinavir, **ritonavir**, and delavirdine and nucleoside reverse...transcriptase inhibitors in patients with HIV/**AIDS** who have failed multiple antiretroviral...efficacy of the combination of indinavir, **ritonavir**, delavirdine, and two NRTIs was examined...193-199 A randomized trial of nelfinavir, **ritonavir**, or delavirdine in combination with...
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☐ **6.** HIV Report November 1997 - Supplement [62K]
Dec 2005
Johns Hopkins **AIDS** Service- Main Navigation 1997...Recommendation Symptomatic (**AIDS**, thrush, unexplained fever...ddI Nelfinavir d4T + ddI **Ritonavir** ZDV + ddC **Ritonavir** + Saquinavir ZDV + 3TC d4T...agents have opposite effects on **CYP 450** pathway and this must be considered...
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☐ **7.** Depression in HIV-infected patients - Allopathic, complementary, and alternative treatments
Fulk, L.J. / Kane, B.E. / Phillips, K.D. / Bopp, C.M. / Hand, G.A., *Journal of Psychosomatic Research*, Oct 2004
...a result of HIV/**AIDS**, and gender [7...of nefazodone and **ritonavir** (a protease transcriptase...example, not only does **ritonavir** exert effects on...have an effect on **CYP-450** isoenzyme-mediated...not interact with **CYP-450** system [27] . May...
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☐ **8.** IAPAC [103K]
Feb 2006
...morbidity and mortality rates. Even before the **AIDS** pandemic, an estimated 50 percent of adults...HIV infection, accounting for a third of **AIDS**-related deaths worldwide. In addition...The Joint United Nations Programme on HIV/**AIDS** (UNAIDS) estimated that out of a global...
[http://www.iapac.org/home.asp?pid=77&toolid=2&itemid=9...]
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☐ **9.** Initiating Antiretroviral Therapy [110K]
Erna M. Kojic / Charles C.J. Carpenter, May 2006
...as a PI (with low-dose **ritonavir**) with an NNRTI and one...concomitant use of low-dose **ritonavir**, which boosts plasma...drugs. **Ritonavir** inhibits **CYP 450** in both the gastrointestinal...enhancement is primarily due to **CYP 450** inhibition in the liver...
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☐ **10.** DRUG - DRUG INTERACTIONS BETWEEN HAART MEDICATIONS USED [PDF-47K]
Aug 2005
...alcohol dependence) Inhibits some **CYP 450** enzymes May interact with ARVs6...generally required. 8. Saquinavir/**Ritonavir AIDS** Clinical Trials Group (ACTG) 401 evaluated the effects of saquinavir/**ritonavir** (400 mg/400 mg) on the pharmacokinetics...
[http://hivguidelines.org/public_html/sub-ddi/sub-ddi.p...]
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11. eMedicine - Incontinence, Urinary: Nonsurgical Therapies : Article by Jong M Choe, MD,

FACS† [180K]
Apr 2006
...neuropathy. Less common causes of overflow incontinence include **AIDS**, genital herpes affecting the perineal area, and neurosyphilis...neuropathy. Less common causes of overflow incontinence include **AIDS**, genital herpes affecting the perineal area, and neurosyphilis...
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12. Microsoft Word - anticonvulsant-int.doc [PDF-29K]
Jul 2005
...enzyme induction potential for **ritonavir** concentrations and/or phenobarbital...patient started in 3TC, ddI, **ritonavir** 600mg BID, and saquinavir...concentrations Topiramate **CYP 450** enzymes no major interaction...12 Potent Enzyme Inhibitors **Ritonavir** - Norvir®13 Lopinavir/**Ritonavir**...
[http://www.tthhivclinic.com/pdf/anticonvulsant-int.pdf]
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13. PowerPoint Presentation [PPT-7MB]
Mar 2006
...Urine In the HIV/**AIDS** patient the diagnosis...cytochrome P450 (**CYP-450**) enzymes which then...Cytochrome P450 (**CYP-450**). Rifampin (& ST. John's Wort) induce **CYP-450** reducing the concentration...NNRTIs. PIs NNRTIs **Ritonavir** Nevirapine Saquinavir...
[http://medicine.nova.edu/academics/clinical/forms/HIVI...]
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14. NIDA - Interactions Between Drugs of Abuse and Pharmacotherapeutic Agents Used in the Treatment of AIDS and Drug Addiction [45K]
May 2006
...their attachment with high affinity. **Ritonavir** is the most potent inhibitor of CYP3A4...with oxygen at the iron site of CYP. **Ritonavir** and nelfinavir, besides inhibiting CYP3A4...isozyme to induce their own metabolism. **Ritonavir** also inhibits CYP2D6. Indinavir, amprenavir...greatly complicate the link between HIV/**AIDS** and substance abuse. HIV PIs and NNRTIs...
[http://www.drugabuse.gov/MeetSum/Interactions.html]
similar results

15. Candida albicans endocarditis treatment with caspofungin in an HIV-infected patient-case report and review of literature
Bacak, V. / Biocina, B. / Starcevic, B. / Gertler, S. / Begovac, J., *Journal of Infection*, Jul 2006
...Begovac a ? josip.begovac@zg.htnet.hr a Department of HIV/**AIDS**, University Hospital for Infectious Diseases, Mirogojska 8...Antiretroviral treatment with stavudine, lamivudine and lopinavir/**ritonavir** was started in April 2004. Discussion We present a case of...expected, as methadone is primarily metabolized by hepatic **CYP 450** enzymes, and caspofungin is not substantially metabolized...
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16. USE OF A COMBINATION CONTAINING A NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR (NNRTI) WITH AN INHIBITOR OF CYTOCHROME...
CORDINGLEY, Michael, Graham / BOEHRINGER INGELHEIM INTERNATIONAL GMBH, *PATENT COOPERATION TREATY APPLICATION*, Jul 2004
...administering either a single **CYP 450** inhibitor or more than one **CYP 450** inhibitor. The invention...acceptable salt, and the **CYP 450** inhibitor or inhibitors...Procedures by which **ritonavir** ((2S,3S,5S)-5-(N-(N...immunodeficiency syndrome (**AIDS**) and related diseases...
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☐ **17.** CLINICAL MANAGEMENT OF [PDF-928K]
Aug 2004
...a collaborative effort of the Southeast **AIDS** Training and Education Center, Department...Infectious Disease Program the Midwest **AIDS** Training and Education Center at the University...Patricia Yeargin, RN, MN, MPH, CANP Southeast **AIDS** Training and Education Center, Emory University...
[http://www.seatec.emory.edu/clinicalprotocols/clinical...]
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☐ **18.** 03Sept_NL_12pg.qxd [PDF-81K]
Sep 2003
...Number 5 The Johns Hopkins University **AIDS** Service September 2003 A bimonthly...other clinical trials suggesting that **ritonavir**-boosted PIs are more potent than unboosted...atazanavir (ATV, Reyataz) with lopinavir/**ritonavir** (LPV/r, Kaletra) were presented at...more impressive in BMS-045, in which **ritonavir**- boosted ATV (ATV/RTV 300/100 mg qd...Director, The Johns Hopkins University **AIDS** Service Richard E. Chaisson, M.D. Professor...
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☐ **19.** Psychotropic drug guide new.qxd (Page 1) [PDF-25K]
Mar 2006
...in patients with advanced **AIDS**. It is best to start with...specific to this combination . **Ritonavir** is a moderately strong 2D6...Kaletra) Nelfinavir (Viracept) **Ritonavir** (Norvir) Saquinavir(Fortovase...in patients with advanced **AIDS**. In these patients, start...NNRTIs. Phenytoin: known to be **CYP 450** 3A4 enzyme inducer, may decrease...Carbamazepine levels increased by **ritonavir** (Kato). Phenytoin: Co-administration...
[http://www.ucsf.edu/sfaetc/resources/CORREFMANUAL/docs...]
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☐ **20.** HAART [PDF-40K]
Jul 2005
...gestación 2.- Basado en IP Lopinavir/**ritonavir** (co-formulación) + (Lamivudina o Emtricitabina...Abacavir o Didanosina) o (Tenofovir + **ritonavir** 100mg/d) Fosamprenavir + (Lamivudina...Tenofovir o Didanosina) Fosamprenavir/**ritonavir** + (Lamivudina o Emtricitabina) + (Zidovudina...
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Feb 1998
...Retroviruses and Opportunistic Infections Chicago, IL - February 1-5, 1998 Ritonavir (RIT) pharmacokinetics (PK) during **combination therapy** with delavirdine (DLV). Conf Retroviruses Opportunistic Infect 1998 Feb 1-5 5th:143 (abstract no. 343) Morse GD...
more hits from [http://www.aegis.com/conferences/CROI/1998/343.html]
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☐ **2.** Incidence of and risk factors for severe hepatotoxicity associated with antiretroviral combination therapy.
Ferdinand W N M Wit / Gerrit Jan Weverling / Jan Weel / Suzanne Jurriaans / Joep M A Lange, *J Infect Dis*, Jul 2002
This retrospective cohort study investigated whether particular antiretroviral agents are associated with a higher risk for developing grade 4 liver enzyme elevations (LEEs) in patients with human immunodeficiency virus (HIV) type 1 infection who are...
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☐ **3.** Recurrent ingrown toenails secondary to indinavir/ritonavir combination therapy.
C W James / K C McNelis / D M Cohen / S Szabo / A K Bincsik, *Ann Pharmacother*, Jul 2001
...indinavir/ritonavir (IDV/RTV) **combination therapy**. CASE SUMMARY: The median...elected to maintain IDV/RTV **combination therapy**. Two patients experienced...receiving ongoing IDV/RTV **combination therapy**. DISCUSSION: IGTN and paronychia...
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☐ **4.** COMBINATION THERAPY FOR THE TREATMENT OF AIDS
VACCA, Joseph, P. / LIN, Jiunn, H. / YEH, Kuang, C. / CHODAKEWITZ, Jeffrey,

A. / DEUTSCH, Paul, J. / JU, William, D. / MERCK & / CO., INC., *EUROPEAN PATENT*, Oct 2000
...present invention provides **combination therapy** for the treatment of HIV...the invention to provide a **combination therapy** which lowers HIV viral levels...Zidovudine and Lamivudine. This **combination therapy** is a method to enhance the...
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☐ **5.** Response to two consecutive protease inhibitor combination therapy regimens in a cohort of HIV-1-infected children.
Gerardo C Palacios / Veronica L Palafox / Maria T Alvarez-Muñoz / Guillermo Vazquez / Guadalupe Miranda / Onofre Muñoz / Fortino Solorzano, *Scand J Infect Dis*, Feb 2002
The response to 2 consecutive protease inhibitor (P1) combination regimens was evaluated in a cohort of HIV-1-infected children. Twelve children, most of whom had been heavily treated, received a 3-drug treatment: saquinavir in hard gelatin capsules...

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☐ **6.** Duration and predictors of CD4 T-cell gains in patients who continue combination therapy despite detectable plasma viremia.
Steven G Deeks / Jason D Barbour / Robert M Grant / Jeffrey N Martin, *AIDS*, Jan 2002
BACKGROUND: Sustained elevations in CD4 cell counts commonly occur despite incomplete viral suppression with protease inhibitor-based antiretroviral therapy. OBJECTIVES: To determine the incidence and risk factors associated with return of CD4 cell...

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☐ **7.** An open-label randomized trial to evaluate different therapeutic strategies of combination therapy in HIV-1 infection:...
Initio Co-ordinating Committee, *Control Clin Trials*, Apr 2001
This article discusses the design of an ongoing open-label, randomized trial comparing three strategies of initial and subsequent HIV therapy in terms of long-term immunological and virological effect. The three treatment arms are (1) didanosine (ddI)...

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☐ **8.** Efficacy and safety of twice daily first-line ritonavir/indinavir plus double nucleoside combination therapy in HIV-infected...
J K Rockstroh / F Bergmann / W Wiesel / A Rieke / A Thiesen / G Fätkenheuer / M Oette / (...) / H Knechten, *AIDS*, Jun 2000
...lamivudine (38%) or stavudine/didanosine (13%) plus ritonavir 400 mg twice daily and indinavir 400 mg twice daily **combination therapy**. CD4 cell counts and HIV RNA were determined at weeks 0, 4, 8, 12, 16, 20, and 24. Statistical analysis was performed...

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☐ **9.** Safety, tolerability, and antiretroviral effects of ritonavir-nelfinavir combination therapy administered for 48 weeks.
C P Raines / C Flexner / E Sun / M Heath-Chiozzi / R H Lewis / C Fields / C Deetz / (...) / J E Gallant, *J Acquir Immune Defic Syndr*, Dec 2000
OBJECTIVE: To evaluate the safety, tolerability, and anti-HIV activity of ritonavir-nelfinavir (RTV-NFV). DESIGN: Single-site, open-label, nonrandomized, multiple-dose trial of RTV combined with two doses of NFV in protease inhibitor (PI)-naive,...

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☐ **10.** Ritonavir combination therapy restores intestinal function in children with advanced HIV disease.
R B Canani / M I Spagnuolo / P Cirillo / A Guarino, *J Acquir Immune Defic Syndr*, Aug 1999
...and after treatment with **combination therapy** that includes ritonavir. To test the hypothesis that **combination therapy** improves intestinal function...months after institution of **combination therapy**. Mean results of each of...

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☐ **11.** Clinical efficacy of protease inhibitor based antiretroviral combination therapy--a prospective cohort study.
B Salzberger / J Rockstroh / U Wieland / C Franzen / A Schwenk / A Jütte / P Hegener / (...) / G Fätkenheuer, *Eur J Med Res*, Nov 1999
...suppression) and PI used (Saquinavir vs. Indinavir or Ritonavir, RR 2.7). CONCLUSIONS: Virological failure of PI based **combination therapy** is common and associated with advanced HIV-infection. Clinical failure is associated with advanced HIV-infection...

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☐ **12.** Ritonavir and saquinavir combination therapy for the treatment of HIV infection.
D W Cameron / A J Japour / Y Xu / A Hsu / J Mellors / C Farthing / C Cohen / (...) / E Sun, *AIDS*, Feb 1999
OBJECTIVE: To evaluate the safety and antiretroviral activity of ritonavir (Norvir) and saquinavir (Invirase) **combination therapy** in patients with HIV infection. DESIGN: A multicenter, randomized, open-label clinical trial. SETTING: Seven HIV...

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☐ **13.** Virtual inhibitory quotient predicts response to ritonavir boosting of indinavir-based therapy in human immunodeficiency...
Nancy Shulman / Andrew Zolopa / Diane Havlir / Ann Hsu / Cheryl Renz / Sheila Boller / Ping Jiang / (...) / Eugene Sun, *Antimicrob Agents Chemother*, Dec 2002
...before the switch and 3 weeks after the switch. **Combination therapy** increased the indinavir predose concentrations...concentration in plasma achieved with indinavir-ritonavir **combination therapy**, was the best predictor of a viral load reduction...

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☐ **14.** Crixivan, Norvir combination therapy studied.
W Strain, *Posit Living*, Apr 1999
Drug Interactions; Drug Therapy, Combination; HIV Infections; HIV Protease Inhibitors; Humans; Indinavir; Ritonavir

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☐ **15.** Application for Inclusion of indinavir/low dose ritonavir on WHO Model List of E [Word-113K]
May 2002
...to IDV in full doses. It is less clear whether **combination therapy** is associated with less toxicity than full dose...Fund, it aims to have 7,000 patients on triple **combination therapy** by the end of 2007. At the end of 2001, an estimated...
[http://www.who.int/medicines/organization/par/edl/indi...]
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☐ **16.** Norvir - Special Populations [14K]
Oct 2002
...are no controlled or adequate studies of Norvir **combination therapy** taken by pregnant women. Norvir should only be...by breastmilk. The safety and benefits of Norvir **combination therapy** has been determined in children between the ages...
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☐ **17.** [Experiences with antiretroviral combination therapy]
U S Justesen / L H Mygind / S S Pedersen / C Pedersen, *Ugeskr Laeger*, Mar 1999
The purpose of the study was to evaluate the efficacy of treating of HIV infected patients with two nucleoside analogues and one protease inhibitor in clinical practice. Sixty-one patients were included and followed with respect to plasma HIV-RNA, CD4...

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☐ **18.** High rebound of plasma and cellular HIV load after discontinuation of triple combination therapy.
V Jubault / M Burgard / E Le Corfec / D Costagliola / C Rouzioux / J P Viard, *AIDS*, Dec 1998
Adult; Anti-HIV Agents; CD4 Lymphocyte Count; DNA, Viral; Dideoxynucleosides; Drug Therapy, Combination; HIV Infections; HIV Protease Inhibitors; HIV-1; Humans; Indinavir; Leukocytes, Mononuclear; Male; Middle Aged; RNA, Viral; Reverse Transcriptase Inhibitors; Ritonavir; Viral Load

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☐ **19.** Combination therapy containing ritonavir plus saquinavir has superior short-term antiretroviral efficacy: a randomized trial.
O Kirk / T L Katzenstein / J Gerstoft / L Mathiesen / H Nielsen / C Pedersen / J D Lundgren, *AIDS*, Jan 1999
OBJECTIVES: To compare the efficacy and safety of indinavir 800 mg three times a day, ritonavir 600 mg twice a day, and a combination of ritonavir 400 mg twice a day and

saquinavir 400 mg twice a day, when administered with two nucleoside analogues....

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20. Combination therapy with indinavir, ritonavir, and delavirdine and nucleoside reverse transcriptase inhibitors in patients...
M Grodesky / E P Acosta / N Fujita / S Mason / J G Gerber, *HIV Clin Trials*, May 2001
PURPOSE: Ritonavir (RTV) and delavirdine (DLV) are inhibitors of cytochrome P450 (CYP) 3A4, the specific CYP that metabolizes indinavir (IDV). We hypothesized that patients who have failed multiple therapies containing protease inhibitors would still...

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Feb 1998
...February 1-5, 1998 Ritonavir (RIT) pharmacokinetics (PK) during **combination therapy** with delavirdine (DLV). Conf Retroviruses Opportunistic...approximately 70%, presumably though inhibition of RIT oxidative **metabolism**. These data provide a rationale for a lower dose of RIT...
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VACCA, Joseph, P. / LIN, Jiunn, H. / YEH, Kuang, C. / CHODAKEWITZ, Jeffrey, A. / DEUTSCH, Paul, J. / JU, William, D. / MERCK & / CO., INC., *EUROPEAN PATENT*, Oct 2000
...invention provides **combination therapy** for the treatment...invention to provide a **combination therapy** which lowers HIV...Lamivudine. This **combination therapy** is a method to enhance...due to extensive **metabolism** by CYPIIIA4 prior...
Full text available at patent office. For more in-depth searching go to LexisNexis
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☐ **3.** Pharmacy Key, May 1996 [11K]
Jun 1998
...zidovudine and zalcitabine as triple **combination therapy** does not effect the absorption, **metabolism** or elimination of any of these drugs...zalcitabine or zidovudine as part of **combination therapy** are 0.75 mg TID and 200 mg TID, respectively... [http://www2.kumc.edu/druginfo/pharmkey/PharmKeyMay96.h...]
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☐ **4.** Application for Inclusion of indinavir/low dose ritonavir on WHO Model List of E [Word-113K]
May 2002
...activity, but because it inhibits the **metabolism** of indinavir. This is sometimes known...full doses. It is less clear whether **combination therapy** is associated with less toxicity than...aims to have 7,000 patients on triple **combination therapy** by the end of 2007. At the end of...

[http://www.who.int/medicines/organization/par/edl/indi...]
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☐ **5.** In-vitro and in-vivo pharmacokinetic interactions of amprenavir, an HIV protease inhibitor, with other current HIV protease...
Nobuhito Shibata / Weihua Gao / Hiroyuki Okamoto / Tomoyuki Kishida / Yukako Yoshikawa / Kanji Takada, *J Pharm Pharmacol*, Feb 2002
...was 0.67, indicating that amprenavir **metabolism** in rat liver microsomes was strongly...other interaction processes besides **metabolism** in the liver. However, these results...of AIDS patients when they receive a **combination therapy** with two kinds of HIV protease inhibitor...

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☐ **6.** Table I [PDF-370K]
Mar 2002
It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the HIV/AIDS Treatment Information Service website (http://www.hivatis.org).
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☐ **7.** RR5107-Front Cover.p65 [PDF-305K]
May 2002
Guidelines for using antiretroviral agents among HIV-infected adults and adolescents: recommendations of the Panel on Clinical Practices for Treatment of HIV. MMWR 2002;51 (No. RR- 7):[inclusive page numbers].
[http://www.cdc.gov/MMWR/PDF/rr/rr5107.pdf]
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☐ **8.** JOURNAL 7/02/YES [PDF-144K]
Dec 2002
...Syndr 200229:340-345. **Combination therapy** with indinavir, ritonavir...the CYP3A4-mediated **metabolism** of protease inhibitors...inducer of delavirdine **metabolism**: A steady state pharmacokinetic...induction of its own **metabolism**. Efavirenz has an...continued PI-based **combination therapy** or were switched from...
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Aug 2002
...ritonavir inhibits the CYP3A-mediated **metabolism** of lopinavir, thereby providing increased...metabolized by CYP3A. Ritonavir inhibits the **metabolism** of lopinavir, thereby increasing the...volunteers and HIV-positive patients. **Metabolism**: In vitro experiments with human hepatic...
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☐ **10.** D.99July_NL_12pg.QRK [PDF-73K]
Sep 1999
...The Hopkins HIV Report July 1999 **Combination therapy** for HIV infection can reduce viral...in patients who are doing well on **combination therapy**. This mechanism involves the establishment...these cells, even in patients on **combination therapy** who have no detectable plasma virus...
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...absorption, transport, distribution, **metabolism**, or excretion of a drug. In therapy...They may involve alterations in drug **metabolism** mediated by the cytochrome P-450 sys...and each of these drugs may alter the **metabolism** of other antiretroviral and concomitantly...
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...villi and can account for first-pass **metabolism** of many drugs. These heme-containing...An increased understanding of drug **metabolism** is solving much of the mystery behind...3A4. When a drug is administered, its **metabolism** via a cytochrome may result in another...
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...well. If this is your experience, the message is clear: as long as you're fol- lowing the general "rules" about 3-drug **combination therapy**, just keep doing what you're doing. If you're one of the lucky few who at least temporarily achieve "un- detectable" viral...
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Mukhopadhyay, A. / Wei, B. / Zullo, S.J. / Wood, L.V. / Weiner, H., *Mitochondrion*, Oct 2002
...involved in the regulation of lipid **metabolism** (Carr et al., 1998a,b). Since lipodystrophy...the introduction of PIs as part of **combination therapy** for HIV infection, it was initially...mitochondrial function such as respiration or **metabolism**, although preliminary experiments in...
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Evolutionary Analysis of HIV-1 Protease Inhibitors: Methods for Design of Inhibitors That Evade Resistance Daniel Stoffler, Michel F. Sanner, Garrett M. Morris, Arthur J. Olson, and David S.
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Ray, J. / Pang, E. / Carey, D., *Journal of Chromatography B, Analytical Technologies in the Biomedical and Life Sciences*, Aug 2002
...inhibits the cytochrome3A-mediated **metabolism** of LOP leading to an increase in

plasma...Potentials coadministered drugs used in **combination therapy** with INV, RTV and LOP, including HIV-reverse...variability in drug absorption, distribution, **metabolism** and excretion. Drug dose is a poor...

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Spengler, U. / Lichterfeld, M. / Rockstroh, J.K., *Journal of Hepatology*, Feb 2002
...liver, particularly when fatty acid **metabolism** is also blocked due to the mitochondrial...it soon became evident that NRTI **combination therapy** carries a considerable risk of causing...agent in patients on antiretroviral **combination therapy** [35,36] . Didanosine seems to be particularly...

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N Shibata / Y Matsumura / H Okamoto / Y Kawaguchi / A Ohtani / Y Yoshikawa / K Takada, *J Pharm Pharmacol*, Oct 2000
...in-vitro data, suggesting the presence of other interaction processes besides **metabolism** in the liver. These results provide useful information for the treatment of AIDS patients receiving **combination therapy** with two HIV-1 protease inhibitors.

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...CYP3A4 may alter intestinal or hepatic **metabolism** of other drugs. The 20-fold increase...inhibi- tion of CYP3A4 at both sites. 20 **Grapefruit** juice con- tains various substances that inhibit CYP3A4-medi- ated **metabolism** only in the wall of the gut, mainly...ing concomitant administration of **grapefruit** juice. 11 However, **grapefruit** juice... [http://www.ecu.edu/intmedresidency/currentresidents/Re...]
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Tapp Alter, K., *Primary Care Update for OB/GYNS*, Mar 2001
...replication process, **combination therapy** provides for...first-pass hepatic **metabolism**. Food also...erythromycin, and **grapefruit** juice. If...part of a **combination therapy**. The elimination...when used in **combination therapy**. 3 Adverse...
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The Case Manager, Sep 1997
...bioavailability Serum half-life Route of **metabolism** Storage Adverse effects Drug interactions...capsule: 4%, erratic 1-2 hours Biliary **metabolism** p450 cytochrome 3A4 Room temperature...increased by ritonavir, ketoconazole, **grapefruit** juice Â Saquinavir levels reduced...alkaloids 20-80% 3.5-5 hours Biliary **metabolism** p450 cytochrome 3A4 Room temperature...
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Lewis, J.S. / Terriff, C.M. / Coulston, D.R. / Garrison, M.W., *Clinical Therapeutics*, Mar 1997
...agents as monotherapy versus use in **combination therapy** with other antiretroviral medications...cell counts and viral loads.12 **Combination Therapy** Significant reductions in viral...monotherapy, zalcitabine monotherapy, and **combination therapy** using the two agents. Saquinavir...
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...saquinavir HGC in **combination therapy** is more effective...medications or with **grapefruit** juice will...when used in **combination therapy**, can achieve...attained with **combination therapy** including...medications or with **grapefruit** juice will...
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